

U. M. Garcia  
10/635808

=> dis his

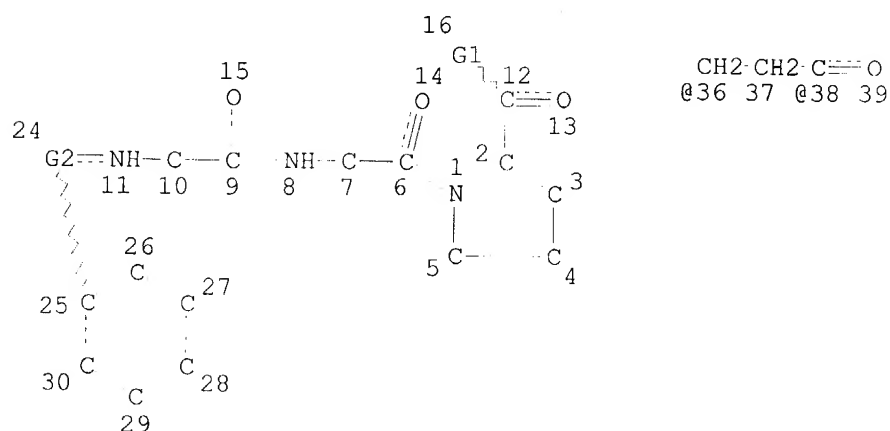
(FILE 'CAOLD' ENTERED AT 10:16:32 ON 28 SEP 2004)  
DEL HIS Y

FILE 'REGISTRY' ENTERED AT 10:16:44 ON 28 SEP 2004

L1 STR  
L2 50 S L1  
L3 STR L1  
L4 1 S L3  
L5 STR L3  
L6 308 S L5 FUL

=> d 16 que stat;fil medl,hcapl,embase,biosis;s 16  
L5 STR

Ak-- NH O Ak Ak N--Ak C=O CH2 C=O  
@17 18 @19 20 21 @22 23 @31 32 @33 @34 35



CH2-CH2-CH2 C=O CH-CH C=O O-CH2-C=O  
@40 41 42 @43 44 @45 46 @47 48 @49 50 @51 52

VAR G1=OH/19/NH2/17/22  
VAR G2=31/33-25 34-11/36-25 38-11/40-25 43-11/45-25 47-11/49-25 51-11  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 52

STEREO ATTRIBUTES: NONE  
L6 308 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED 294255 ITERATIONS  
SEARCH TIME: 00.00.27

308 ANSWERS

COST IN U.S. DOLLARS  
FULL ESTIMATED COST

SINCE FILE  
ENTRY  
166.34  
TOTAL  
SESSION  
690.09

Searched by: Mary Hale 571-272-2507 REM 1D86

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| CA SUBSCRIBER PRICE                        | 0.00             | -37.10        |

FILE 'MEDLINE' ENTERED AT 10:33:09 ON 28 SEP 2004

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|     |                  |
|-----|------------------|
| L7  | 44 FILE MEDLINE  |
| L8  | 174 FILE HCAPLUS |
| L9  | 16 FILE EMBASE   |
| L10 | 0 FILE BIOSIS    |

TOTAL FOR ALL FILES  
 L11 234 L6

=> s l11 and (postlesion? or post lesion? or neurodegenerat? or neurolog? degen? or alzheimer? or dement? or cognitive impairment or neural trauma)

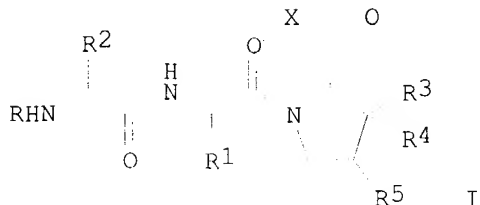
|     |                |
|-----|----------------|
| L12 | 0 FILE MEDLINE |
| L13 | 3 FILE HCAPLUS |
| L14 | 0 FILE EMBASE  |
| L15 | 0 FILE BIOSIS  |

TOTAL FOR ALL FILES  
 L16 3 L11 AND (POSTLESION? OR POST LESION? OR NEURODEGENERAT? OR NEUROLOG? DEGEN? OR ALZHEIMER? OR DEMENT? OR COGNITIVE IMPAIRMENT OR NEURAL TRAUMA)

=> d 1-3 cbib abs hitstr

L16 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN  
 2002:609522 Document No. 137:163818 Tripeptide derivatives for the treatment of **post-lesional** diseases of the nervous system.  
 Rapin, Jean; Witzmann, Hans Klaus; Grumel, Jean-Marie; Gonella, Jacques (Tell-Pharm AG, Switz.). Ger. Offen. DE 10105040 A1 20020814, 4 pp.  
 (German). CODEN: GWXXBX. APPLICATION: DE 2001-10105040 20010205.

GI



AB The invention discloses the use of cinnamoyl tripeptide derivs. for the

Searched by: Mary Hale 571-272-2507 REM 1D86

treatment of **post-lesional** neuronal diseases. The cinnamoyl tripeptide derivs. are I [X = OH, Cl-5 alkoxy, NH<sub>2</sub>, NH(Cl-5 alkyl), N(Cl-5 alkyl)<sub>2</sub>; R = (preferably) cinnamoyl; R<sub>1</sub> = group derived from Phe, Tyr, Trp, Pro, Ala, Val, Leu or Ile; R<sub>2</sub> = group derived from Gly, Ala, Ile, Val, Ser, Thr, His, Arg, Lys, Pro, Glu, Gln, pGlu, Asp and Asn; R<sub>3</sub>, R<sub>4</sub> = H, OH, Cl-5 alkyl, Cl-5 alkoxy, provided that R<sub>3</sub> and R<sub>4</sub> are not both OH or Cl-5 alkoxy; R<sub>5</sub> = H, OH, Cl-5 alkyl, Cl-5 alkoxy], or a pharmaceutical acceptable salt thereof.

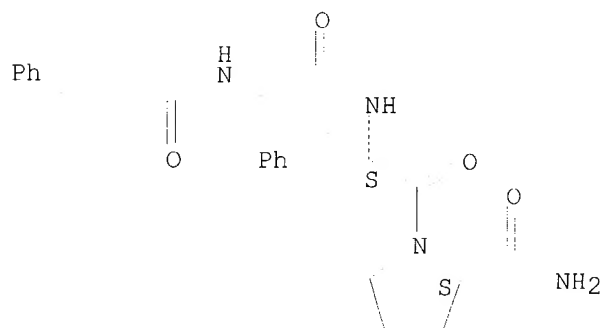
IT 123910-57-6

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tripeptide derivs. for treatment of **post-lesional** nervous system diseases)

RN 123910-57-6 HCAPLUS

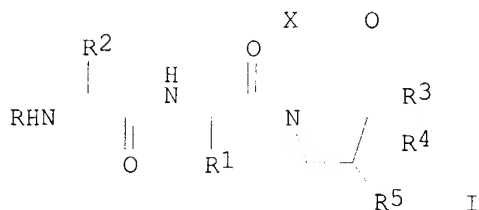
CN L-Prolinamide, N-(1-oxo-3-phenyl-2-propenyl)glycyl-L-phenylalanyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



L16 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN  
2002:591566 Document No. 137:135103 Tripeptide derivatives for treatment of **neurodegenerative** diseases. Rapin, Jean; Witzmann, Hans Klaus; Grumel, Jean-Marie; Gonella, Jacques (Tell-Pharm A.-G., Switz.). Ger. Offen. DE 10105039 A1 20020808, 10 pp. (German). CODEN: GWXXBX.  
APPLICATION: DE 2001-10105039 20010205.

GI



AB The invention discloses the use of tripeptide derivs. for treatment of **neurodegenerative** diseases. The tripeptide derivs. are I [X = OH, Cl-5 alkoxy, NH<sub>2</sub>, NH(Cl-5 alkyl), N(Cl-5 alkyl)<sub>2</sub>; R = (preferably) cinnamoyl; R<sub>1</sub> = group derived from Phe, Tyr, Trp, Pro, Ala, Val, Leu or Ile; R<sub>2</sub> = group derived from Gly, Ala, Ile, Val, Ser, Thr, His, Arg, Lys,

Pro, Glu, Gln, pGlu, Asp or Asn; R3, R4 = H, OH, C1-5 alkyl, C1-5 alkoxy, provided that R3 and R4 are not both OH or C1-5 alkoxy; R5 = H, OH, C1-5 alkyl, C1-5 alkoxy], or a pharmaceutically compatible salt. Cinnamoyl-Gly-L-Phe-L-Pro-NH2 was tested in an **Alzheimer's** disease model.

IT 123910-57-6

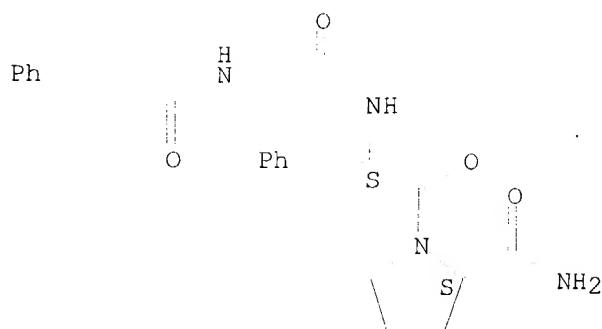
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tripeptide derivs. for treatment of **neurodegenerative** diseases)

RN 123910-57-6 HCAPLUS

CN L-Prolinamide, N-(1-oxo-3-phenyl-2-propenyl)glycyl-L-phenylalanyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



L16 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

1989:633680 Document No. 111:233680 Preparation of tripeptides containing L-proline derivatives as nootropics and pharmaceutical compositions containing them. Fiez-Vandal, Pierre Yves (Inorgan S. A., Switz.). Eur. Pat. Appl. EP 316218 A1 19890517, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE. (French). CODEN: EPXXDW. APPLICATION: EP 1988-402761 19881103. PRIORITY: FR 1987-15228 19871103.

GI



AB The title compds. [I; R1 = Q; X = CO, YCO, OYCO; Y = alkylene, alkenylene; Z = H, ≥1 CF3, alkyl, alkylenedioxy; R2 = NH2, OH, or a functional derivative thereof; A1, A2 = amino acid residue; B1, B2 = H, Me] and their pharmaceutically acceptable salts, useful as nootropics for treatment of senile **dementia**, **Alzheimer's** disease, Parkinson's disease, schizophrenia, and depression, are prepared via reaction of activated R1-A1-OH with proline derivs. II (R3 = H-A2), obtained by reaction of II (R3 = H) with activated H-A2-OH. N-Cinnamoylglycine (preparation given) was condensed with II.CF3CO2H (R2 = NH2, B1 = B2 = H, R3 = H-Phe) (preparation given) in DMF containing dicyclohexylcarbodiimide and N-methylmorpholine to give I (R1 = cinnamoyl, R2 = NH2, B1 = B2 = H, A1 =

Gly, A2 = Phe) (III). III, administered i.p. or p.o. at 1 mg/kg, was effective in antagonizing scopolamine-induced amnesia in mice.

IT 123910-50-9P 123910-52-1P 123910-53-2P  
123910-54-3P 123910-55-4P 123910-56-5P  
123910-57-6P 123910-58-7P

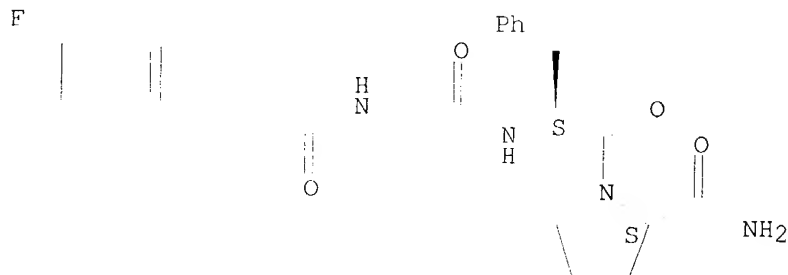
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as nootropic)

RN 123910-50-9 HCAPLUS

CN L-Prolinamide, N-[3-(4-fluorophenyl)-1-oxo-2-propenyl]glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

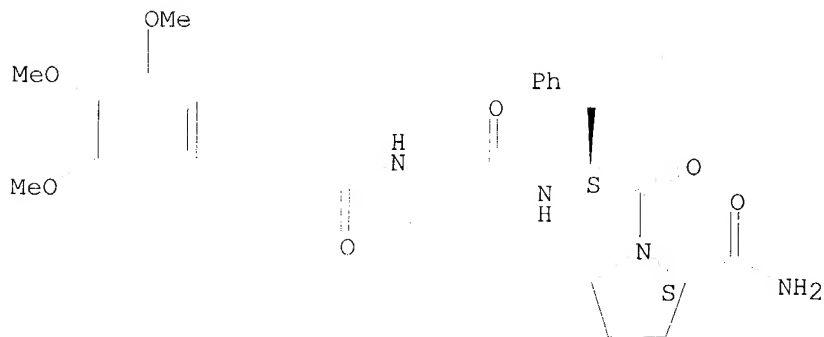


RN 123910-52-1 HCAPLUS

CN L-Prolinamide, N-[1-oxo-3-(3,4,5-trimethoxyphenyl)-2-propenyl]glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

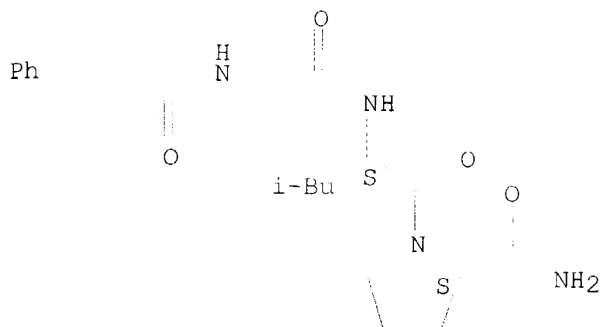


RN 123910-53-2 HCAPLUS

CN L-Prolinamide, N-(1-oxo-3-phenyl-2-propenyl)glycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

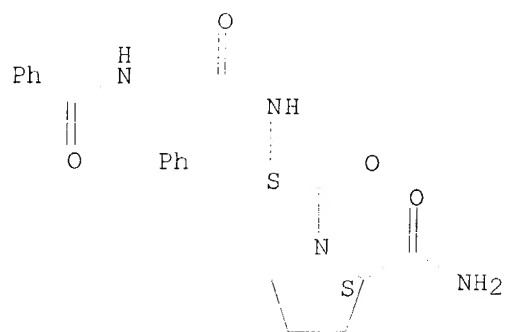
Double bond geometry unknown.



RN 123910-54-3 HCAPLUS

CN L-Prolinamide, N-benzoylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

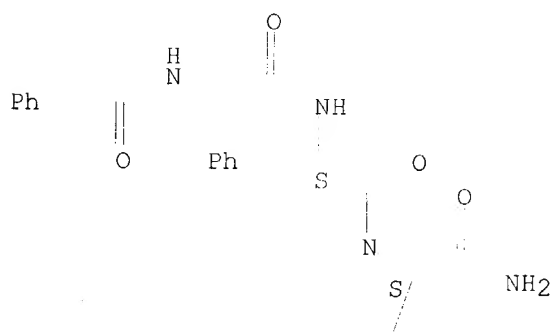
Absolute stereochemistry.



RN 123910-55-4 HCAPLUS

CN L-Prolinamide, N-(phenylacetyl)glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

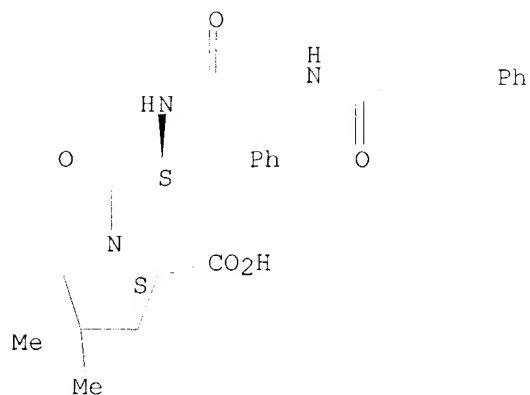


RN 123910-56-5 HCAPLUS

CN L-Proline, 4,4-dimethyl-1-[N-[N-(1-oxo-3-phenyl-2-propenyl)glycyl]-L-phenylalanyl]- (9CI) (CA INDEX NAME)

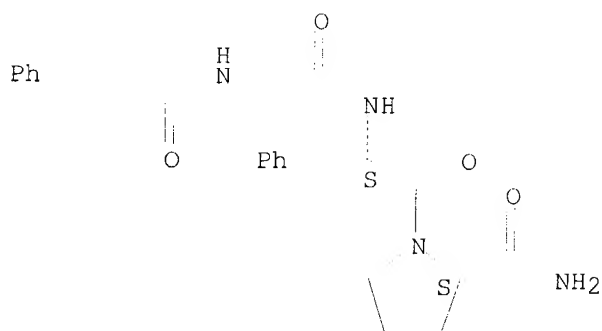
Absolute stereochemistry.

Double bond geometry unknown.



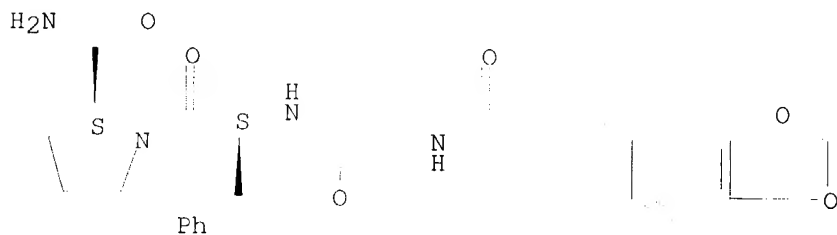
RN 123910-57-6 HCAPLUS  
 CN L-Prolinamide, N-(1-oxo-3-phenyl-2-propenyl)glycyl-L-phenylalanyl- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



RN 123910-58-7 HCAPLUS  
 CN L-Prolinamide, N-[3-(1,3-benzodioxol-5-yl)-1-oxo-2-propenyl]glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



=> fil hcapl;e postlesional/ct  
 COST IN U.S. DOLLARS  
 FULL ESTIMATED COST

| SINCE FILE | TOTAL   |
|------------|---------|
| ENTRY      | SESSION |
| 38.79      | 728.88  |

Searched by: Mary Hale 571-272-2507 REM 1D86

|  |            |         |
|--|------------|---------|
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL   |
|  | ENTRY      | SESSION |
| CA SUBSCRIBER PRICE                        | -2.10      | -39.20  |

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FILE COVERS 1907 - 28 Sep 2004 VOL 141 ISS 14  
 FILE LAST UPDATED: 27 Sep 2004 (20040927/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

| E#  | FREQUENCY | AT  | TERM  |
|-----|-----------|-----|---|
| --  | -----     | --  | ----  |
| E1  | 0         | 1   | POSTIMPLANTATION/CT                           |
| E2  | 0         | 2   | POSTIMPLANTATION EMBRYO/CT                    |
| E3  | 0         | --> | POSTLESIONAL/CT                               |
| E4  | 0         | 1   | POSTMENOPAUSAL/CT                             |
| E5  | 0         | 2   | POSTMENOPAUSAL BONE LOSS/CT                   |
| E6  | 0         | 2   | POSTMENOPAUSAL HORMONE REPLACEMENT THERAPY/CT |
| E7  | 0         | 2   | POSTMENOPAUSAL OSTEOPOROSIS/CT                |
| E8  | 0         | 2   | POSTMENOPAUSE/CT                              |
| E9  | 0         | 1   | POSTMORTEM/CT                                 |
| E10 | 0         | 2   | POSTMORTEM HUMAN TISSUE/CT                    |
| E11 | 0         | 1   | POSTNATAL/CT                                  |
| E12 | 0         | 2   | POSTNATAL DEPRESSION/CT                       |

=> e neurodegenerative/ct

| E#  | FREQUENCY | AT    | TERM                            |
|-----|-----------|-------|---------------------------------|
| --  | -----     | --    | ----                            |
| E1  | 0         | 1     | NEUROD3/CT                      |
| E2  | 0         | 2     | NEURODEGENERATION/CT            |
| E3  | 0         | 1 --> | NEURODEGENERATIVE/CT            |
| E4  | 0         | 2     | NEURODEGENERATIVE DISEASE/CT    |
| E5  | 0         | 2     | NEURODEGENERATIVE DISEASES/CT   |
| E6  | 0         | 2     | NEURODEGENERATIVE DISORDER/CT   |
| E7  | 0         | 2     | NEURODEGENERATIVE DISORDERS/CT  |
| E8  | 0         | 2     | NEURODERMATITIS/CT              |
| E9  | 1         |       | NEURODIA CYCLOPION FLORIDANA/CT |
| E10 | 0         | 2     | NEUROECTODERM/CT                |
| E11 | 0         | 2     | NEUROECTODERM NEOPLASM/CT       |
| E12 | 0         | 2     | NEUROECTODERM TUMORS/CT         |

=> e e3+all

E1 0 --> Neurodegenerative/CT  
 \*\*\*\*\* END \*\*\*\*\*



=> e alzheimer?/ct

| E#  | FREQUENCY | AT  | TERM                                     |
|-----|-----------|-----|--|
| E1  | 0         | 1   | ALZHEIMER-TYPE/CT                        |
| E2  | 0         | 2   | ALZHEIMER-TYPE SENILE DEMENTIA/CT        |
| E3  | 0         | --> | ALZHEIMER?/CT                            |
| E4  | 0         | 1   | AM/CT                                    |
| E5  | 0         | 2   | AM 0.5/CT                                |
| E6  | 0         | 2   | AM 1002/CT                               |
| E7  | 0         | 2   | AM 100L/CT                               |
| E8  | 0         | 2   | AM 111/CT                                |
| E9  | 0         | 2   | AM 2000UP/CT                             |
| E10 | 0         | 2   | AM 6/CT                                  |
| E11 | 0         | 2   | AM BLACK/CT                              |
| E12 | 0         | 2   | AM MICROBIAL GENE AND GENETIC ELEMENT/CT |

=> e alzheimers/ct

| E#  | FREQUENCY | AT  | TERM                                     |
|-----|-----------|-----|--|
| E1  | 0         | 1   | ALZHEIMER-TYPE/CT                        |
| E2  | 0         | 2   | ALZHEIMER-TYPE SENILE DEMENTIA/CT        |
| E3  | 0         | --> | ALZHEIMERS/CT                            |
| E4  | 0         | 1   | AM/CT                                    |
| E5  | 0         | 2   | AM 0.5/CT                                |
| E6  | 0         | 2   | AM 1002/CT                               |
| E7  | 0         | 2   | AM 100L/CT                               |
| E8  | 0         | 2   | AM 111/CT                                |
| E9  | 0         | 2   | AM 2000UP/CT                             |
| E10 | 0         | 2   | AM 6/CT                                  |
| E11 | 0         | 2   | AM BLACK/CT                              |
| E12 | 0         | 2   | AM MICROBIAL GENE AND GENETIC ELEMENT/CT |

=> e cognitive impairment/ct

| E#  | FREQUENCY | AT | TERM                         |
|-----|-----------|----|------------------------------|
| E1  | 0         | 2  | COGNITIVE BEHAVIOR/CT        |
| E2  | 0         | 3  | COGNITIVE DISORDERS/CT       |
| E3  | 0         | 3  | --> COGNITIVE IMPAIRMENT/CT  |
| E4  | 0         | 3  | COGNITIVE MENTAL DISORDER/CT |
| E5  | 0         | 1  | COGON/CT                     |
| E6  | 0         | 2  | COGON GRASS/CT               |
| E7  | 2         |    | COGWHEELS/CT                 |
| E8  | 0         | 1  | COH/CT                       |
| E9  | 0         | 1  | COHAERENS/CT                 |
| E10 | 0         | 1  | COHEN/CT                     |
| E11 | 2         | 2  | COHEN SYNDROME/CT            |
| E12 | 9         |    | COHEN, ERNST/CT              |

=> e e3+all

|                 |   |     |                                      |
|-----------------|---|-----|--------------------------------------|
| E1              | 0 | --> | Cognitive impairment/CT              |
| E2              |   |     | USE Cognition (L) disorder/CT        |
| E3              |   |     | USE Mental disorder (L) cognitive/CT |
| ***** END ***** |   |     |                                      |

=> e neural trauma/ct

| E# | FREQUENCY | AT  | TERM   |
|----|-----------|-----|--|
| E1 | 0         | 2   | NEURAL TISSUE-SPECIFIC F-ACTIN-BINDING PROTEINS/CT |
| E2 | 0         | 3   | NEURAL TRANSPLANT/CT                               |
| E3 | 0         | --> | NEURAL TRAUMA/CT                                   |
| E4 | 0         | 2   | NEURAL TUBE/CT                                     |

|     |    |   |  |
|-----|----|---|--|
| E5  | 0  | 2 | NEURAL TUBE DEFECT/CT  |
| E6  | 0  | 2 | NEURAL TUBE DEFECTS/CT                                       |
| E7  | 0  | 2 | NEURAL TUBE DISEASE/CT                                       |
| E8  | 0  | 2 | NEURAL TUBE NERVOUS SYSTEM/CT                                |
| E9  | 0  | 2 | NEURAL TUMORS/CT   |
| E10 | 0  | 1 | NEURAL-/CT   |
| E11 | 0  | 2 | NEURAL- AND THYMUS-DERIVED ACTIVATOR FOR ERBB KINASES/<br>CT |
| E12 | 55 | 2 | NEURALGIA/CT   |

=> fil medl,hcapl,embase,biosis;s l11 and (mental disorder(l)cognitive or cognition(l)disorder)

|                      |            |         |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL   |
|                      | ENTRY      | SESSION |
| FULL ESTIMATED COST  | 7.08       | 735.96  |

|  |            |         |
|--|------------|---------|
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL   |
|  | ENTRY      | SESSION |
| CA SUBSCRIBER PRICE                        | 0.00       | -39.20  |

FILE 'MEDLINE' ENTERED AT 10:38:28 ON 28 SEP 2004

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|     |   |              |
|-----|---|--------------|
| L17 | 0 | FILE MEDLINE |
| L18 | 0 | FILE HCAPLUS |
| L19 | 0 | FILE EMBASE  |
| L20 | 0 | FILE BIOSIS  |

TOTAL FOR ALL FILES

|     |   |   |
|-----|---|---|
| L21 | 0 | L11 AND (MENTAL DISORDER(L) COGNITIVE OR COGNITION(L) DISORDER) |
|-----|---|---|

=> s rapin, j?/au;s witzmann, h?/au;s grumel, j?/au;s gonella, j?/au

|     |     |              |
|-----|-----|--------------|
| L22 | 114 | FILE MEDLINE |
| L23 | 166 | FILE HCAPLUS |
| L24 | 131 | FILE EMBASE  |
| L25 | 149 | FILE BIOSIS  |

TOTAL FOR ALL FILES

|     |     |              |
|-----|-----|--------------|
| L26 | 560 | RAPIN, J?/AU |
|-----|-----|--------------|

|     |     |              |
|-----|-----|--------------|
| L27 | 3   | FILE MEDLINE |
| L28 | 134 | FILE HCAPLUS |
| L29 | 3   | FILE EMBASE  |
| L30 | 3   | FILE BIOSIS  |

TOTAL FOR ALL FILES

|     |     |                 |
|-----|-----|-----------------|
| L31 | 143 | WITZMANN, H?/AU |
|-----|-----|-----------------|

|     |   |              |
|-----|---|--------------|
| L32 | 0 | FILE MEDLINE |
|-----|---|--------------|

L33 4 FILE HCAPLUS  
L34 2 FILE EMBASE  
L35 1 FILE BIOSIS

TOTAL FOR ALL FILES

L36 7 GRUMEL, J?/AU

L37 45 FILE MEDLINE  
L38 38 FILE HCAPLUS  
L39 29 FILE EMBASE  
L40 47 FILE BIOSIS

TOTAL FOR ALL FILES

L41 159 GONELLA, J?/AU

=> s 126 and 131 and 136 and 141

L42 0 FILE MEDLINE  
L43 4 FILE HCAPLUS  
L44 0 FILE EMBASE  
L45 0 FILE BIOSIS

TOTAL FOR ALL FILES

L46 4 L26 AND L31 AND L36 AND L41

=> d 1-4 cbib abs;fil reg

L46 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

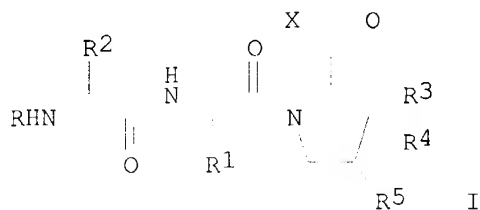
2002:609523 Document No. 137:155181 Synthesis of tripeptides and tripeptide derivatives for the treatment of neurodegenerative diseases. **Rapin, Jean; Witzmann, Hans Klaus; Grumel, Jean-Marie; Gonella, Jacques** (Tell-Pharm Ag, Switz.). Ger. Offen. DE 10105041 A1 20020814, 12 pp. (German). CODEN: GWXXBX. APPLICATION: DE 2001-10105041 20010205.

AB The invention concerns the use of tripeptide derivs. [e.g., H-Gly-Phe-Pro-NH<sub>2</sub> (I)] for the treatment of neurodegenerative disease, such as Alzheimer's disease. Thus, Boc-Phe-OH [Boc = (CH<sub>3</sub>)<sub>3</sub>OC(O)] was coupled with TFA.H-Pro-NH<sub>2</sub> to give a dipeptide, which was N-deprotected and converted to its TFA salt for coupling with Boc-Gly-OH; the resulting protected tripeptide was N-deprotected and converted to its HCl salt. The blood-brain partition coeffs. of I and seventeen similar tripeptides were given. The plasma half-life of <sup>14</sup>C-labeled I.HCl was determined in rats (no data). Using a rat model of Alzheimer's disease, results of treatment with I showed retention of learned behavior in a five-day test of pole-climbing at a signal to avoid shock. Examination of subject brains revealed increase dendrite development in the hippocampus.

L46 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

2002:609522 Document No. 137:163818 Tripeptide derivatives for the treatment of post-lesional diseases of the nervous system. **Rapin, Jean; Witzmann, Hans Klaus; Grumel, Jean-Marie; Gonella, Jacques** (Tell-Pharm AG, Switz.). Ger. Offen. DE 10105040 A1 20020814, 4 pp. (German). CODEN: GWXXBX. APPLICATION: DE 2001-10105040 20010205.

GI



AB The invention discloses the use of cinnamoyl tripeptide derivs. for the treatment of post-lesional neuronal diseases. The cinnamoyl tripeptide derivs. are I [X = OH, C1-5 alkoxy, NH<sub>2</sub>, NH(C1-5 alkyl), N(C1-5 alkyl)<sub>2</sub>; R = (preferably) cinnamoyl; R1 = group derived from Phe, Tyr, Trp, Pro, Ala, Val, Leu or Ile; R2 = group derived from Gly, Ala, Ile, Val, Ser, Thr, His, Arg, Lys, Pro, Glu, Gln, pGlu, Asp and Asn; R3, R4 = H, OH, C1-5 alkyl, C1-5 alkoxy, provided that R3 and R4 are not both OH or C1-5 alkoxy; R5 = H, OH, C1-5 alkyl, C1-5 alkoxy], or a pharmaceutical acceptable salt thereof.

L46 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

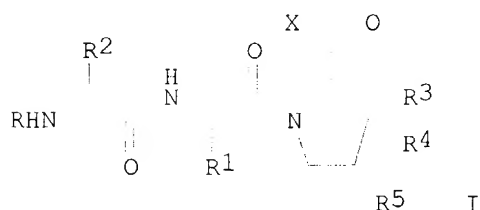
2002:609521 Document No. 137:140781 Synthesis of tripeptides and tripeptide derivatives for the treatment of post lesional diseases of the nervous system.. **Rapin, Jean; Witzmann, Hans Klaus; Grumel, Jean-Marie; Gonella, Jacques** (Tell-Pharm Ag, Switz.). Ger. Offen. DE 10105038 A1 20020814, 10 pp. (German). CODEN: GWXXBX. APPLICATION: DE 2001-10105038 20010205.

AB The invention concerns the use of tripeptide derivs. [e.g., H-Gly-Phe-Pro-NH<sub>2</sub> (I)] for the treatment of post lesional diseases of the nervous system. Thus, Boc-Phe-OH [Boc = (CH<sub>3</sub>)<sub>3</sub>OC(O)] was coupled with TFA.H-Pro-NH<sub>2</sub> to give a dipeptide, which was N-deprotected and converted to its TFA salt for coupling with Boc-Gly-OH; the resulting protected tripeptide was N-deprotected and converted to its HCl salt. The blood-brain partition coeffs. of I and seventeen similar tripeptides were given. The plasma half-life of <sup>14</sup>C-labeled I.HCl was determined in rats (no data). Using an in-vivo dendritic sprouting assay in rats, I was tested for effect on hippocampus septum, and showed growth of up to 2µm, compared to controls.

L46 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

2002:591566 Document No. 137:135103 Tripeptide derivatives for treatment of neurodegenerative diseases. **Rapin, Jean; Witzmann, Hans Klaus; Grumel, Jean-Marie; Gonella, Jacques** (Tell-Pharm A.-G., Switz.). Ger. Offen. DE 10105039 A1 20020808, 10 pp. (German). CODEN: GWXXBX. APPLICATION: DE 2001-10105039 20010205.

GI



AB The invention discloses the use of tripeptide derivs. for treatment of neurodegenerative diseases. The tripeptide derivs. are I [X = OH, C1-5 alkoxy, NH<sub>2</sub>, NH(C1-5 alkyl), N(C1-5 alkyl)<sub>2</sub>; R = (preferably) cinnamoyl; R1 = group derived from Phe, Tyr, Trp, Pro, Ala, Val, Leu or Ile; R2 = group derived from Gly, Ala, Ile, Val, Ser, Thr, His, Arg, Lys, Pro, Glu, Gln, pGlu, Asp or Asn; R3, R4 = H, OH, C1-5 alkyl, C1-5 alkoxy, provided that R3 and R4 are not both OH or C1-5 alkoxy; R5 = H, OH, C1-5 alkyl, C1-5 alkoxy], or a pharmaceutically compatible salt. Cinnamoyl-Gly-L-Phe-L-Pro-NH<sub>2</sub> was tested in an Alzheimer's disease model.

|  |            |         |
|--|------------|---------|
| COST IN U.S. DOLLARS                       | SINCE FILE | TOTAL   |
|  | ENTRY      | SESSION |
| FULL ESTIMATED COST                        | 15.01      | 750.97  |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL   |
|  | ENTRY      | SESSION |
| CA SUBSCRIBER PRICE                        | -2.80      | -42.00  |

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 DICTIONARY FILE UPDATES: 27 SEP 2004 HIGHEST RN 752974-11-1

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<http://www.cas.org/ONLINE/DBSS/registryss.html>

```
=> e "cinnamoyl-glycyl-l-phenylalanyl-l-prolinamide"/cn
E1      1      CINNAMOYL-COA: (R)-PHENYLACTATE COA-TRANSFERASE/CN
E2      1      CINNAMOYL-COENZYME A REDUCTASE/CN
E3      0 --> CINNAMOYL-GLYCYL-L-PHENYLALANYL-L-PROLINAMIDE/CN
E4      1      CINNAMOYLACETALDEHYDE/CN
E5      1      CINNAMOYLACETONE/CN
E6      1      CINNAMOYLACETONITRILE/CN
E7      1      CINNAMOYLAUBUCIN/CN
E8      1      CINNAMOYLAUCUBIN/CN
E9      1      CINNAMOYLCHOLINE/CN
E10     1      CINNAMOYLCHOLINE CHLORIDE/CN
E11     1      CINNAMOYLCOCAINE/CN
E12     1      CINNAMOYLDIAMINOPIPERAZINE/CN

=>
=> e
E13     1      CINNAMOYLECGONINE/CN
E14     1      CINNAMOYLECGONINE METHYL ESTER/CN
```

|     |   |  |
|-----|---|--|
| E15 | 1 | CINNAMOYLETHYL METHACRYLATE-DIMETHYLOCTYLAMMONIUM STYRENESULFONATE-METHACRYLIC ACID-TRIS (TRIMETHYLSILOXY) (3- (METHACRYLOYLOXY) PROPYL) SILANE COPOLYMER/CN |
| E16 | 1 | CINNAMOYLETHYL METHACRYLATE-STYRENE BLOCK COPOLYMER/CN   |
| E17 | 1 | CINNAMOYLFERROCENE/CN  |
| E18 | 1 | CINNAMOYLGLUCOSE-ALCOHOL CINNAMOYLTRANSFERASE/CN   |
| E19 | 1 | CINNAMOYLGLYCINE/CN  |
| E20 | 1 | CINNAMOYLGLYCINE P-NITROPHENYL ESTER/CN  |
| E21 | 1 | CINNAMOYLGRANDIFLORIC ACID/CN  |
| E22 | 1 | CINNAMOYLHYDRAZINE/CN  |
| E23 | 1 | CINNAMOYLHYDROXAMIC ACID/CN  |
| E24 | 1 | CINNAMOYL IUM/CN   |

```
=> s cinnamoyl(1)glycyl(1)phenylalanyl(1)prolinamide
      3686 CINNAMOYL
        1 CINNAMOYLS
      3686 CINNAMOYL
          (CINNAMOYL OR CINNAMOYLS)
      492293 GLYCYL
        2 GLYCYLS
      492293 GLYCYL
          (GLYCYL OR GLYCYLS)
      367484 PHENYLALANYL
        21527 PROLINAMIDE
L47      0 CINNAMOYL (L) GLYCYL (L) PHENYLALANYL (L) PROLINAMIDE
```

```
=> e "cinnamoyl-isoleucyl-phenylalanyl-l-proline ethylamide"/cn
E1      1 CINNAMOYL-COA: (R)-PHENYLLACTATE COA-TRANSFERASE/CN
E2      1 CINNAMOYL-COENZYME A REDUCTASE/CN
E3      0 --> CINNAMOYL-ISOLEUCYL-PHENYLALANYL-L-PROLINE ETHYLAMIDE/CN
E4      1 CINNAMOYLACETALDEHYDE/CN
E5      1 CINNAMOYLACETONE/CN
E6      1 CINNAMOYLACETONITRILE/CN
E7      1 CINNAMOYLAUBUCIN/CN
E8      1 CINNAMOYLAUCUBIN/CN
E9      1 CINNAMOYLCHOLINE/CN
E10     1 CINNAMOYLCHOLINE CHLORIDE/CN
E11     1 CINNAMOYLCOCAINE/CN
E12     1 CINNAMOYLDIAMINOPIPERAZINE/CN
```

```
=> s cinnamoyl(1)isoleucyl(1)phenylalanyl(1)proline(1)ethylamide
      3686 CINNAMOYL
        1 CINNAMOYLS
      3686 CINNAMOYL
          (CINNAMOYL OR CINNAMOYLS)
      325112 ISOLEUCYL
      367484 PHENYLALANYL
        85965 PROLINE
          2 PROLINES
        85965 PROLINE
          (PROLINE OR PROLINES)
        621 ETHYLAMIDE
L48      0 CINNAMOYL (L) ISOLEUCYL (L) PHENYLALANYL (L) PROLINE (L) ETHYLAMIDE
```

```
=> e "cinnamoyl-isoleucyl-isoleucyl-prolineamide"/cn
E1      1 CINNAMOYL-COA: (R)-PHENYLLACTATE COA-TRANSFERASE/CN
E2      1 CINNAMOYL-COENZYME A REDUCTASE/CN
E3      0 --> CINNAMOYL-ISOLEUCYL-ISOLEUCYL-PROLINEAMIDE/CN
E4      1 CINNAMOYLACETALDEHYDE/CN
E5      1 CINNAMOYLACETONE/CN
E6      1 CINNAMOYLACETONITRILE/CN
E7      1 CINNAMOYLAUBUCIN/CN
```

E8 1 CINNAMOYL AUCUBIN/CN  
 E9 1 CINNAMOYL CHOLINE/CN  
 E10 1 CINNAMOYL CHOLINE CHLORIDE/CN  
 E11 1 CINNAMOYL COCAINE/CN  
 E12 1 CINNAMOYL DIAMINOPIPERAZINE/CN

=> s cinnamoyl(1)isoleucyl(1)isoleucyl(1)prolineamide  
 3686 CINNAMOYL  
 1 CINNAMOYLS  
 3686 CINNAMOYL  
 (CINNAMOYL OR CINNAMOYLS)  
 325112 ISOLEUCYL  
 325112 ISOLEUCYL  
 2 PROLINEAMIDE  
 L49 0 CINNAMOYL(L) ISOLEUCYL(L) ISOLEUCYL(L) PROLINEAMIDE

|  |            |         |
|--|------------|---------|
| => fil medl,hcap,biosis,embase,wpids       |            |         |
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| FULL ESTIMATED COST                        | 59.69      | 810.66  |
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|  | ENTRY      | SESSION |
| CA SUBSCRIBER PRICE                        | 0.00       | -42.00  |

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=> s cinnamoyl(1)isoleucyl(1)isoleucyl(1)prolineamide  
 L50 0 FILE MEDLINE  
 L51 0 FILE HCAPLUS  
 L52 0 FILE BIOSIS  
 L53 0 FILE EMBASE  
 L54 0 FILE WPIDS

TOTAL FOR ALL FILES  
 L55 0 CINNAMOYL(L) ISOLEUCYL(L) ISOLEUCYL(L) PROLINEAMIDE

=> s cinnamoyl(1)isoleucyl(1)phenylalanyl(1)proline(1)ethylamide  
 L56 0 FILE MEDLINE  
 L57 0 FILE HCAPLUS  
 L58 0 FILE BIOSIS  
 L59 0 FILE EMBASE  
 L60 0 FILE WPIDS

TOTAL FOR ALL FILES  
 L61 0 CINNAMOYL(L) ISOLEUCYL(L) PHENYLALANYL(L) PROLINE(L) ETHYLAMIDE

=> s cinnamoyl(1)glycyl(1)phenylalanyl(1)prolinamide

L62 0 FILE MEDLINE  
L63 0 FILE HCAPLUS  
L64 0 FILE BIOSIS  
L65 0 FILE EMBASE  
L66 1 FILE WPIDS

TOTAL FOR ALL FILES

L67 1 CINNAMOYL(L) GLYCYL(L) PHENYLALANYL(L) PROLINAMIDE

=> d

L67 ANSWER 1 OF 1 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN  
AN 2002-667977 [72] WPIDS  
DNC C2002-187773  
TI Use of proline-containing tripeptide for treating neurodegeneration,  
useful particularly in early stages of Alzheimer's disease.  
DC B02 B03  
IN GONELLA, J; GRUMEL, J; RAPIN, J; WITZMANN, H K  
PA (TELL-N) TELL-PHARM AG; (NEUR-N) NEUROTOLL AG  
CYC 101  
PI DE 10105039 A1 20020808 (200272)\* 10 A61K038-06  
WO 2002062830 A1 20020815 (200272) EN C07K005-08  
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NL OA PT SD SE SL SZ TR TZ UG ZM ZW  
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DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM  
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EP 1358204 A1 20031105 (200377) EN C07K005-08  
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AU 2002247685 A1 20020819 (200427) C07K005-08  
ADT DE 10105039 A1 DE 2001-10105039 20010205; WO 2002062830 A1 WO 2002-EP1181  
20020205; EP 1358204 A1 EP 2002-716727 20020205, WO 2002-EP1181 20020205;  
AU 2002247685 A1 AU 2002-247685 20020205  
FDT EP 1358204 A1 Based on WO 2002062830; AU 2002247685 A1 Based on WO  
2002062830  
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IC ICM A61K038-06; C07K005-08  
ICS A61P025-28

=> fil reg

COST IN U.S. DOLLARS

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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE | TOTAL   |
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| ENTRY      | SESSION |
| 0.00       | -42.00  |

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Searched by: Mary Hale 571-272-2507 REM 1D86



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<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> del his y

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